REMARKS

In this Amendment, Applicant has cancelled Claims 1 – 16 without prejudice or disclaimer and added new Claims 17 – 27. Claims 17 – 27 have been added to specify various embodiments of the present invention and overcome the rejection. It is respectfully submitted that no new matter has been introduced by the amended claims. All claims are now present for examination and favorable reconsideration is respectfully requested in view of the preceding amendments and the following comments.

REJECTIONS UNDER 35 U.S.C. § 101:

Claims 1 – 16 have been rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter.

It is respectfully submitted that the presently added new Claims 17 – 27 are directed to the patenable statutory subject matter. More specifically, Claim 17 has been added to recite specific step in practicing the claimed invention. Claims 18 – 26 include the step by their dependency on Claim 17. In addition, the term "isolated *H. pylori* thioredoxin protein" has been added in Claims 17 and 26.

Therefore, the currently presented Claims 17 – 27 are directed to statutory subject matter and the rejection under 35 U.S.C. § 101 has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 101 is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 102:

Claims 1 – 7 and 15 – 16 have been rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Tomb et al. (1997), hereinafter Tomb, or Alm et al (1999) (SWISS-Prot accession number P56430), hereinafter Alm. Claims 1 – 9, 12 – 13 and 15 – 16 have been rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by White et al. (US 5,985,261), hereinafter White, as evidenced by Zhang et al. (1999),

hereinafter Zhang. Claims 1 – 2, 4 – 6, 8 – 9 and 11 have been rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Yoshida et al. (1999), hereinafter Yoshida, as evidence by Swiss Prot accession number P10599, hereinafter P10599.

Applicant traverses the rejection and respectfully submits that the present-claimed invention is not anticipated by the cited reference. At first, Claims 1 – 16 have been cancelled. The rejection to these claims is moot. It is respectfully submitted that there are significant differences between the cited references and the currently presented Claims 17 – 27. The present invention relates to the use of isolated thioredoxin from *Helicobacter pylori* rather than other sources of thioredoxin for use as an anti-inflammatory agent. Most of the thioredoxins described in the cited prior art appear to have the opposite effect to the *H. pylori* thioredoxin of the present invention in that they increase or induce NFκB DNA binding or induce nuclear translocation of NFκB. In contrast, the *H. pylori* thioredoxin of the present invention inhibits NFκB DNA-binding.

Tomb and Alm describe the complete annotation (sequencing) of the *H. pylori* genome obtained from two different strains. These papers disclose 'lists' of all the genes in the bacterium. The genes, where appropriate, are assigned names based on homology to genes of similar sequence from other organisms. Tomb and Alm only indicates to a person of ordinary skill in the art that the named genes are similar to other genes with known functions. It doesn't mean that the genes have identical roles in different organisms. This can only be confirmed/tested by studying the gene/gene product in isolation, using biochemical and molecular biological methods. It is respectfully submitted that there is no disclosure or indication in Tomb or Alm to the function of the genes described.

Zhang describes a reduction in thioredoxin in lung cells/tissue associated with a reduction in NFκB DNA binding activity. In this instance, the authors of Zhang are referring to mammalian thioredoxin (human, murine) rather than prokaryotic thioredoxin. The authors in Zhang state that a reduction in the amount of thioredoxin is associated with a reduction in the NFκB DNA binding activity. In contrast, in the present invention,

Applicant indicates that by adding exogenous prokaryotic thioredoxin, Applicant can achieve a reduction in the amount of NFκB DNA-binding activity (see examples 1 to 5).

White describes the effect of *E. coli* thioredoxin on MnSOD levels in lung adenocarcinoma cells. In this case, they show that externally added *E. coli* thioredoxin increases the amount of intracellular MnSOD and thereby protects the cells from oxidative damage. The authors of White anticipate that thioredoxin could thus be used to treat various lung diseases including ARDS and asthma. However, White fails to describe the effect of *E. coli* thioredoxin on NFκB DNA-binding activity in the lung cells in vitro. In addition, there is no evidence showing whether the mode of action of *E. coli* and *H. pylori* thioredoxins is the same. There is no teaching or suggestion that they would both represent efficacious therapeutic entities to treat lung disease (as described by White) or other NFκB-mediated inflammatory disease states.

The *E. coli* thioredoxin described in White appears to enter the lung cell line whereas *H. pylori* thioredoxin appears to be unable to enter gastric epithelial cell lines. There could be many reasons for this difference. For example, it could be due to differences in the cell lines used, the experimental approach/method, or due to differences in the species of thioredoxin used. It is not clear from White exactly which *E. coli* thioredoxin was used in the experiment described. It is known that *E. coli* has more than one thioredoxin. Furthermore, it is known that different thioredoxins from different species have different functions.

In addition, it is respectfully submitted that the Examiner is incorrect in the interpretation of Yoshida. Yoshida describes the work carried out by using human thioredoxin (epitopes of human TRX, ADF11 and ADF21 and recombinant human TRX (page 352 second column) rather than *H. pylori* thioredoxin. Furthermore, the experiments in Yoshida demonstrate that human thioredoxin, when added exogeneously to cells treated with a proinflammatory cytokine (TNF), induces NFκB DNA binding activity. In contrast, in the present invention, Applicant describes how *H. pylori* thioredoxin inhibits NFκB DNA binding activity. Applicant respectfully submits that

even though both molecules may have the same redox active site (CGPC), it is clear to a person of ordinary skill in the art that there is a difference in the mechanism of action of *H. pylori* thioredoxin compared to human thioredoxin.

Moreover, the Swiss Prot accession number P10599 relates to a human derived thioredoxin protein. The human and *H. pylori* thioredoxins are only 27% identical at the amino acid level. Generally, this level of identity is considered low. The fact that the molecules are 73% different indicates that the conformation adopted in the native molecules is also likely to be different, a feature that could impart significant functionally different capabilities to the molecules.

Lastly, the Examiner considers US 6,605,278 to be also pertinent. However, US 6,605,278 describes human TRANK, a thioredoxin peroxidase-related activator of NFκB and c-Jun N-terminal kinase. This protein has little or no homology to *H. pylori* thioredoxin. At best, a gapped alignment yields only 12 % homology. Therefore, US 6,605,278 is irrelevant to the present invention as amended.

In summary, there is no disclosure or suggestion of the features of the present invention as defined. Therefore, the newly presented claim is not anticipated by Coffey and the rejection under 35 U.S.C. § 102 (b) has been overcome. Accordingly, withdrawal of the rejection under 35 U.S.C. § 102 (b) is respectfully requested. Having overcome all outstanding grounds of rejection, the application is now in condition for allowance, and prompt action toward that end is respectfully solicited.

Respectfully submitted,

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